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(FILE 'HOME' ENTERED AT 14:41:29 ON 13 JUL 2007)

919 S L7 OR L8 OR L9 0 S L2 AND L10

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 14:42:13 ON 13 JUL 2007 13234 S BLOOD (A) SUBSTITUTE? L1L2 224 S CONJUGATED (A) HEMOGLOBIN? 59596 S HSA OR (HUMAN (W) SERUM (W) ALBUMIN) L3L45 S L2 AND L3 4 DUP REM L4 (1 DUPLICATE REMOVED) L5 · 2 S ALBUMIN (W) HEMOGLOBIN (W) CONJUGAT? L6 E SU Z/AU L7 909 S E3 E XIULING L/AU 7 S E3 L8E CHUNYANG Z/AU E YUHONG X/AU L9 3 S E3

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=> s conjugated (a)hemoglobin? L2 224 CONJUGATED (A) HEMOGLOBIN?

=> s hSA or (human (w)serum (w)albumin)
L3 59596 HSA OR (HUMAN (W) SERUM (W) ALBUMIN)

=> s 12 and 13

L4 5 L2 AND L3

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PROCESSING COMPLETED FOR L4

L5 4 DUP REM L4 (1 DUPLICATE REMOVED)

=> d 1-4 ibib ab

L5 ANSWER 1 OF 4 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2007127303 EMBASE

TITLE: Engineering blood cells and proteins as blood substitutes:

A short review.

AUTHOR: Kim H.W.

CORPORATE SOURCE: H.W. Kim, Biopure Corp.,, 11 Hurley Street, Cambridge, MA

02141, United States. Hae Kim@Brown.edu

SOURCE: Biotechnology and Bioprocess Engineering, (2007) Vol. 12,

No. 1, pp. 43-47. .

Refs: 30

ISSN: 1226-8372 Korea, Republic of

DOCUMENT TYPE:

COUNTRY:

Journal; General Review

025 Hematology

FILE SEGMENT:

Biophysics, Bioengineering and Medical 027

Instrumentation

037 Drug Literature Index

039 Pharmacy

LANGUAGE: SUMMARY LANGUAGE: English English

ENTRY DATE:

Entered STN: 30 Mar 2007

Last Updated on STN: 30 Mar 2007

In this brief review, basic principles and recent progresses on the AB development of therapeutic substitutes for major blood components are briefly discussed with primary focus on the red cell substitute. .COPYRGT. KSBB.

ANSWER 2 OF 4 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER:

2006:86173 BIOSIS

DOCUMENT NUMBER:

PREV200600077521

TITLE: AUTHOR(S): Extreme hemodilution with PEG-hemoglobin vs. PEG-albumin. Cabrales, Pedro [Reprint Author]; Tsai, Amy G.; Winslow,

Robert M.; Intaglietta, Marcos

CORPORATE SOURCE:

La Jolla Bioengn Inst, 505 Coast Blvd S, Suite 405, La

Jolla, CA 92037 USA pcabrales@ucsd.edu

SOURCE:

American Journal of Physiology - Heart and Circulatory Physiology, (DEC 2005) Vol. 289, No. 6, pp. H2392-H2400.

ISSN: 0363-6135.

DOCUMENT TYPE:

Article English

LANGUAGE: ENTRY DATE:

Entered STN: 25 Jan 2006

Last Updated on STN: 25 Jan 2006

Isovolemic hemodilution to 11% systemic hematocrit was performed in the hamster window chamber model using 6% dextran 70 kDa (Dx 70) and 5% human serum albumin (HSA). Systemic and microvascular effects of these solutions were compared with polyethylene glycol (PEG)-conjugated 5% albumin (MPA) and PEG-conjugated 4.2% Hb (MP4). These studies were performed for the purpose of comparing systemic and microvascular responses of PEG vs. non-PEG plasma expanders and similar oxygen-carrying vs. noncarrying blood replacement fluids.

Mean arterial blood pressure was statistically significantly reduced for all groups compared with baseline (P < 0.05), HSA, MPA, and MP4 higher than Dx 70 (P < 0.05). MP4 and MPA had a significantly higher cardiac index than HSA and Dx 70, in addition to a positive base excess. Microvascular blood flow and capillary perfusion were significantly higher for the PEG compounds compared with HSA and Dx 70. Intravascular PO2 for MP4 and MPA was higher in arterioles (P < 0.05) compared with HSA and Dx 70, but there was no difference in either tissue or venular PO2 between groups. Total Hb in the MP4 group was 4.8 +/- 0.4 g/dl, whereas the remaining groups had a range of 3.6-3.8 g/dl. The hemodilution results showed that PEG compounds maintained microvascular conditions with lower concentrations than conventional plasma expanders. Furthermore, microvascular oxygen delivery and extraction in the window chamber tissue were significantly higher for the PEG compounds. MP4 was significantly higher than MPA (P < 0.05) and was not statistically different from baseline, an effect due to the additional oxygen release to the tissue by the Hb MP4.

ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2005:571260 HCAPLUS

DOCUMENT NUMBER:

143:90623

TITLE:

Conjugate of bovine hemoglobin and human

serum albumin as a candidate for

blood substitute: Characteristics and effects on rats Lu, Xiu-Ling; Zheng, Chun-Yang; Shi, Xiao-Dong; Wang,

Yong-Quan; Suo, Xiao-Yan; Yu, Peng-Zhan; Xu, Yu-Hong;

Ma, Tie-Min; Su, Zhi-Guo

National Key Laboratory of Biochemical Engineering, CORPORATE SOURCE:

Institute of Process Engineering, Chinese Academy of

Sciences, Beijing, Peop. Rep. China

Artificial Cells, Blood Substitutes, and Biotechnology SOURCE:

(2005), 33(2), 83-99

CODEN: ACBSDA

PUBLISHER: Taylor & Francis, Inc.

DOCUMENT TYPE:

AUTHOR (S):

Journal

LANGUAGE: English

Conjugate of bovine Hb (bHb) and human serum

albumin (HSA) was prepared The product was simply

composed of 89.7% one-to-one Hb-HSA conjugate, 6.0% oligomer of

Hb and HSA, 3.5% unconjugated HSA and 0.8%

unconjugated Hb, with an average mol. weight of 157 kD. The physicochem. characteristics were determined Effects of single replacement on blood pressure and long-term survival of rats with 30% and 60% acute blood loss were studied, in comparison with Ringer-lactate solution, stroma-free Hb (SFHb), 5% HSA in Ringer-lactate, whole blood and no

resuscitation fluid. Results showed that Hb-HSA conjugate maintained the mean arterial pressure of rats to initial level with no pressor effect. Long-term effects of the replacement fluids on 30% bleeding rats showed that, for the group infused with Hb-HSA

conjugate, histol. of five major organs, heart, kidney, liver, spleen and lung, were essentially normal, similar to that of whole blood, while obviously. Renal side-effects appeared in other groups. The efficacy of the conjugate was further demonstrated by the resuscitation of lethal hemorrhagic shock rats (60% acute blood loss) with 100% survival rate (followed for 14 days), the same result as whole blood. The Hb-

HSA conjugate can thus be another candidate for blood substitute in emergency.

REFERENCE COUNT:

THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS 24 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 4 OF 4 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

DUPLICATE 1

ACCESSION NUMBER: 2000:119605 BIOSIS DOCUMENT NUMBER: PREV200000119605

TITLE:

Synthesis and physicochemical characterization of a series of hemoglobin-based oxygen carriers: Objective comparison

between cellular and acellular types.

Sakai, Hiromi; Yuasa, Minako; Onuma, Hiroto; Takeoka, AUTHOR (S):

Shinji; Tsuchida, Eishun [Reprint author]

CORPORATE SOURCE: Department of Polymer Chemistry, Advanced Research

Institute for Science and Engineering, Waseda University,

Tokyo, 169-8555, Japan

Bioconjugate Chemistry, (Jan.-Feb., 2000) Vol. 11, No. 1, SOURCE:

pp. 56-64. print.

CODEN: BCCHES. ISSN: 1043-1802.

DOCUMENT TYPE:

Article

LANGUAGE:

English

ENTRY DATE:

Entered STN: 29 Mar 2000

Last Updated on STN: 3 Jan 2002

A series of hemoglobin (Hb)-based O2 carriers, acellular and cellular types, were synthesized and their physicochemical characteristics were compared. The acellular type includes intramolecularly cross-linked Hb (XLHb), polyoxyethylene (POE)-conjugated pyridoxalated Hb (POE-PLP-Hb), hydroxyethylstarch-conjugated Hb (HES-XLHb), and glutaraldehydepolymerized XLHb (Poly-XLHb). The cellular type is Hb-vesicles (HbV) of

which the surface is modified with POE (POE-HbV). Their particle

diameters are 7 +- 2, 22 +- 2, 47 +- 17, 68 +- 24, and 224 +- 76 nm, respectively, thus all the materials penetrate across membrane filters with 0.4 mum pore size, though only the POE-HbV cannot penetrate across the filter with 0.2 mum pore size. These characteristics of permeability are important to consider an optimal particle size in microcirculation in vivo. POE-PLP-Hb ((Hb) = 5 g/dL) showed viscosity of 6.1 cP at 332 s-1 and colloid osmotic pressure (COP) of 70.2 Torr, which are beyond the physiological conditions (human blood, viscosity = 3-4 cP, COP = ca. 25 Torr). XLHb and Poly-XLHb showed viscosities of 1.0 and 1.5 cp, respectively, which are significantly lower than that of blood. COP of POE-HbV is regulated to 20 Torr in 5% human serum albumin (HSA). HES-XLHb and POE-HbV/HSA showed comparable viscosity with human blood. Microscopic observation of human red blood cells (RBC) after mixing blood with POE-PLP-Hb or HES-XLHb disclosed aggregates of RBC, a kind of sludge, indicating a strong interaction with RBC, which is anticipated to modify peripheral blood flow in vivo. On the other hand, XLHb and POE-HbV showed no rouleaux or aggregates of RBC. The acellular Hbs (P50 = 14-32 Torr) have their specific O2 affinities determined by their structures, while that of the cellular POE-HbV is regulated by coencapsulating an appropriate amount of an allosteric effector (e.g., P50 = 18, 32 Torr). These differences in physicochemical characteristics between the acellular and cellular types indicate the advantages of the cellular type from the physiological points of view.

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FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 14:42:13 ON 13 JUL 2007

L1 13234 S BLOOD (A) SUBSTITUTE?

L2 224 S CONJUGATED (A) HEMOGLOBIN?

L3 59596 S HSA OR (HUMAN (W) SERUM (W) ALBUMIN)

L4 5 S L2 AND L3

L5 4 DUP REM L4 (1 DUPLICATE REMOVED)

=> s albumin (w) hemoglobin (w) conjugat?

L6 2 ALBUMIN (W) HEMOGLOBIN (W) CONJUGAT?

=> d 1-2 ibib ab

L6 ANSWER 1 OF 2 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights

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ACCESSION NUMBER: 2002420677 EMBASE

TITLE: A solid phase adsorption method for preparation of bovine

serum albumin-bovine hemoglobin conjugate.

AUTHOR: Hu T.; Su Z.

CORPORATE SOURCE: Z. Su, National Lab. Biochemical Eng., Institute of Process

Engineering, Chinese Academy of Sciences, P.O. Box 353,

Beijing 100080, China. zgsu@home.ipe.ac.cn

SOURCE: Journal of Biotechnology, (13 Feb 2003) Vol. 100, No. 3,

pp. 267-275. .

Refs: 17

ISSN: 0168-1656 CODEN: JBITD4

PUBLISHER IDENT.: S 0168-1656(02)00246-8

COUNTRY: Ne

Netherlands Journal; Article

DOCUMENT TYPE: Journal; Article FILE SEGMENT: 004 Microbiology

027 Biophysics, Bioengineering and Medical

Instrumentation

LANGUAGE: English SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 12 Dec 2002

Last Updated on STN: 12 Dec 2002

As solid phase adsorption method was proposed to prepare well-defined bovine serum albumin-bovine hemoglobin (Hb) conjugate. After adsorption by the solid phase, Q Sepharose Fast Flow media, bovine serum albumin (BSA) molecules were allowed to react with glutaraldehyde. The spacing out of BSA molecules on the solid phase was assumed to limit polymerization of BSA molecules, except some molecules bound closely on the solid phase resulting in minor dimer formation. Following the elution procedure, the activated monomeric BSA was separated from the dimers by gel filtration chromatography on Superdex 200 and then reacted with bovine Hb at 4°C and pH 9.5. The 1:1 (BSA:Hb) conjugate was obtained with the yield of 64%. The P(50) values of the conjugates, prepared under anaerobic and aerobic conditions, were 19.1 and 14.2 mmHg, respectively. The dependence of the P(50) on chloride ions for the conjugate was slightly diminished, presumably due to covalent attachment of BSA to bovine Hb. .COPYRGT. 2002 Elsevier Science B.V. All rights reserved.

L6 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:872226 HCAPLUS

DOCUMENT NUMBER: 138:270350

TITLE: A solid phase adsorption method for preparation of

bovine serum albumin-bovine hemoglobin conjugate

AUTHOR(S): Hu, Tao; Su, Zhiguo

CORPORATE SOURCE: Institute of Process Engineering, National Laboratory

of Biochemical Engineering, Chinese Academy of Sciences, Beijing, 100080, Peop. Rep. China

SOURCE: Journal of Biotechnology (2003), 100(3), 267-275

CODEN: JBITD4; ISSN: 0168-1656

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal LANGUAGE: English

As solid phase adsorption method was proposed to prepare well-defined bovine serum albumin-bovine Hb conjugate. After adsorption by the solid phase, Q Sepharose Fast Flow media, bovine serum albumin (BSA) mols. were allowed to react with glutaraldehyde. The spacing out of BSA mols. on the solid phase was assumed to limit polymerization of BSA mols., except some mols. bound closely on the solid phase resulting in minor dimer formation. Following the elution procedure, the activated monomeric BSA was separated from the dimers by gel filtration chromatog. on Superdex 200 and then reacted with bovine Hb at 4 °C and pH 9.5. The 1:1 (BSA:Hb) conjugate was obtained with the yield of 64%. The P50 values of the conjugates, prepared under anaerobic and aerobic conditions, were 19.1 and 14.2 mmHg, resp. The dependence of the P50 on chloride ions for the conjugate was slightly diminished, presumably due to covalent attachment of BSA to bovine Hb.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L1 13234 S BLOOD (A) SUBSTITUTE?

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L11

0 S L2 AND L10

	Document	Kind	Codes	Source	Issue Date	Page s	Title
1	US 2006024742 3 Al			US- PGPUB	20061102	11	Hemoglobin conjugate and the preparation method and its use

	Document ID	Kind Codes	Source	Issue Date	Page s	Title
1	US 2004025976 9 A1		US- PGPUB	20041223	57	Reduced side-effect hemoglobin compositions
2	US 2003021940 6 A1		US- PGPUB	20031127	4.4	Beta-2-glycoprotein is an inhibitor of angiogenesis
3	US 7211560 B2	٠.	USPAT	20070501	55	Reduced side-effect hemoglobin compositions
4	US 6670323 B1		USPAT	20031230	1	Reduced side-effect hemoglobin compositions
5	US 6458762 B1		USPAT	20021001	15	Therapeutic use of hemoglobin for preserving tissue viability and reducing restenosis
6	US 6117838 A		USPAT	20000912	12	Use of hemoglobin in the treatment of hypotension
7	US 6090779 A		USPAT	20000718	10	Use of hemoglobin to treat septic shock
8	US 6046161 A		USPAT	20000404	10	Use of hemoglobin in the treatment of cardiogenic shock
9	US 6022850 A		USPAT	20000208	10	Use of hemoglobin in the treatment of- stroke
10	US 5945033 A		USPAT	19990831	65	Method for making non-crosslinked protein particles for therapeutic and diagnostic use
11	US 5900477 A		USPAT	19990504	10	Use of hemoglobin in the treatment of hemorrhagic shock
12	US 5877146 A		USPAT	19990302	10	Therapeutic use of hemoglobin in the treatment of blood vessel blockage

13	US 5773417 A		USPAT	19980630	19	Human serum albumin- porphyrin complexes with the ability to bind oxygen and therapeutic uses thereof
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	Document ID	Kind Codes	Source	Issue Date	Page • s	Title
14	US 5733546 A		USPAT	19980331	28	Immunochemical detection of in vivo advanced glycosylation endproducts
IT 2	US 5712101 A	te.	USPAT	19980127		Immunochemical detection of in vivo advanced glycosylation endproducts
16	US 5702704 A		USPAT	19971230		Antibodies to in vivo advanced glycosylation endproducts
17	US 5683887 A		USPAT	19971104	28	Immunochemical detection of in vivo advanced glycosylation endproducts
18	US 5629408 A		USPÄT	19970513	28	Immunochemical isolation of in vivo advanced glycosylation endproducts
19	US 5624804 A		USPAT	19970429	29.	Immunochemical detection of In vivo advanced glycosylation end products
20	US 5616311 A		USPAT	19970401	25	Non-crosslinked protein particles for therapeutic and diagnostic use
21	US 5614490 A		USPAT	19970325	11	Administration of low dose hemoglobin to increase perfusion
22	US 5512268 A		USPAT	19960430	21	Polymeric shells for medical imaging prepared from synthetic polymers, and methods for the use thereof
23	US 5510464 A		USPAT	19960423	11	Administration of low dose hemoglobin to increase perfusion

	Document ID	Kind Codes	Source	Issue Date	Page s	Title
24	US 5508021 A		USPAT	19960416	20	Non-fluorinated polymeric shells for medical imaging
25	US 5505932 A		USPAT	19960409		Method for the preparation of fluorocarbon-containing polymeric shells for medical imaging
26	US 5334706 A		USPAT	19940802	11	Administration of low dose hemoglobin to increase perfusion

	Document ID	Kind Codes	Source	Issue Date	Page s	Title
1	US 2006024742 3 Al		US- PGPUB	20061102		Hemoglobin conjugate and the preparation method and its use
2	US 2005004862 7 A1		US- PGPUB	20050303	21	Human serum albumin- TIMP2 fusion protein, a polynucleotide encoding the same and a method of producing the human serum albumin-TIMP2 fusion protein
3	US 2003021940 6 A1		US- PGPUB	20031127	44	Beta-2-glycoprotein is an inhibitor of angiogenesis
4	US 7163805 B2		USPAT	20070116		Human serum albumin- TIMP2 fusion protein, a polynucleotide encoding the same and a method of producing the human serum albumin-TIMP2 fusion protein
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